



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#14

Applicant: Koster et al.

Serial No.: 09/171,625

Filed: July 2, 1999

For: A COMBINATORIAL PROTECTING
GROUP STRATEGY FOR
MULTIFUNCTIONAL MOLECULES

Art Unit: 1627

Examiner: Ponnaluri, P.

I hereby certify that this paper and the attached papers are being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Commissioner for Patents,
Washington, D.C. 20231, on this date.

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**PETITION UNDER 37 C.F.R. §1.144
PETITION FROM REQUIREMENT FOR RESTRICTION**

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Applicant hereby petitions under 37 C.F.R. §1.144 from a final Lack of Unity Objection ("the Objection") in the above-captioned application. Applicant requests removal of the Objection as between Groups I and IV. Applicant respectfully requests that Groups I and IV be combined for examination in this application.

STATEMENT OF FACTS

The Objection was set forth in a written action, mailed September 5, 2000. The Objection set forth four (4) Groups for election. Applicant elected, with traverse, Group I in an Election, mailed November 28, 2000. Applicant requested reconsideration of the Objection as between Groups I and IV, and as between Groups II and III, in the Election. Applicant's arguments were not deemed persuasive. The Objection was made final in an Office Action, mailed February 26, 2001.

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ARGUMENT

LACK OF UNITY OF INVENTION

Applicant respectfully petitions for reconsideration and removal of the Lack of Unity Objection as between Groups I and IV in view of the following remarks. In addition, it is respectfully submitted that the finality of this holding is premature.

Group I, claims 1, 3, 4 and 11-16, is directed to a process of generating a combinatorial set of core molecules of core structure M and a combinatorial set of compounds with core structure M. Group IV, claims 23-35, is directed to a combinatorial set of compounds with core structure M.

PCT Rule 13

This application is the U.S. national stage of International Patent Application No. PCT/US97/06509, in accordance with 35 U.S.C. §371. Applicant notes that no lack of unity objection was raised during either Chapter I or II at the international stage.

As stated in MPEP 201, national stage applications of international applications are similar to national applications, but there are differences. Among these differences is inapplicability of restriction practice to national stage applications. Restriction practice is applied to national applications, but unity of invention practice is applied to national stage applications (see, MPEP 201 and MPEP 1893.03(d)). Therefore, the applicable rule with respect to the instant national stage application is PCT Rule 13.1.

Lack of Unity Standard

When the U.S. Patent Office considers an international application during the national stage, restriction must be based on unity of invention, which is governed by PCT Rule 13 (see MPEP 1893.03(d); Caterpillar Tractor Co. v. Commissioner of Patents and Trademark, 650 F. Supp. 218, 31 USPQ 590 (E.D. Virginia, 1986); In re Caterpillar Tractor Co., 228 USPQ 77). In the Caterpillar cases it was ultimately held that the language in Rule 13.1 "specially

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adapted" is not to be interpreted as meaning that the process of manufacture can only be used to manufacture the product because this interpretation is in conflict with the PCT Rule, which provides that no national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided in the Treaty (Article 27 of the PCT). Thus, the U.S. Patent Office cannot impose requirements that differ from those provided in the Treaty. Since restriction practice differs from and is more restrictive than unity of invention, the unity of invention rules must govern.

Therefore, it is respectfully submitted, and it appears that the Office has acknowledged, that the rules of unity of invention (PCT Rule 13.1 and 37 C.F.R. §1.475) apply to this application. Rule 13.1 requires that an international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

Groups I and IV do not lack unity under PCT Rule 13

It is respectfully submitted that Groups I and IV relate to a product and a process for the manufacture of said product, and therefore do not lack unity of invention under PCT Rule 13.

Groups I and IV are directed to a process for generating a combinatorial set of molecules of core structure M, and a combinatorial set of compounds with core structure M, respectively. Such groups of claims do not lack unity of invention under PCT Rules 13.1 and 13.2. See 37 CFR §1.475(b):

An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product...

The claims of Group IV are directed to a product (a combinatorial set of compounds with core structure M), and the claims of Group I are directed to a

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process for the manufacture of the product (a process for generating a combinatorial set of molecules of core structure M). Such Groups of claims do not lack unity of invention, and therefore should be examined in one application.

Applicant respectfully requests reconsideration of the lack of unity objection as between Groups I and IV. In view of Applicant's election of Group I, it is respectfully requested that the claims of Groups I and IV, i.e., claims 1, 3, 4, 11-16 and 23-36, be examined in the instant application.

See also, the sixth paragraph of MPEP 1893.93(d):

A process is "specially adapted" for the manufacture of a product if the claimed process inherently produces the claimed product with the technical relationship being present between the claimed process and the claimed product. The expression "specially adapted" does not imply that the product could not also be manufactured by a different process.

Lack of Novelty of Group I

While appearing to agree with the above, the Office Action alleges that the claims of Groups I and IV lack unity of invention because the claims of Group I allegedly are not novel. Applicant respectfully disagrees.

The Office Action, mailed February 26, 2001, urges that the Objection is based on the allegation that synthesis of combinatorial libraries of compounds using solid supports and blocking groups is well known in the art. As stated in the Office Action:

The traversal is on the ground(s) that the special technical feature of group I is not taught by the prior art. This is not found persuasive. Applicants point out that Carell et al. do not teach combinatorial synthesis based on immobilized molecules. Applicants arguments have been considered. However, it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups. Thus, the inventions lack unity.

The Office Action does not dispute Applicant's argument that Carell et al., cited previously by the Office, does not anticipate Group I, and therefore does not destroy the unity of invention as between Groups I and IV. The Office Action alleges that the subject matter of the claims of Group I is well known in the art and therefore lacks novelty. Applicant respectfully disagrees. The

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Office Action fails to cite any art relating to the novelty of the claims of Group I. The Office Action improperly relies on a bare assertion to allege lack of novelty of the claims of Group I.

The Office Action improperly relies on a bare allegation

The Office Action provides no support for the bare allegation that "it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups." As stated in MPEP 2144.03, citing in re Ahlert, 424 F.2d 1088, 1091, 165 USPQ 418,420-421 (CCPA 1970), "[A]ssertions of technical facts in areas of esoteric technology must always be supported by citation of some reference work" and "allegations concerning specific 'knowledge' of the prior art, which might be peculiar to a particular art should also be supported." No support for the allegation that "it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups" is provided. Applicant respectfully requests that the Examiner provide support for the allegation.

The claims of Group I are novel over the bare assertion of the Office Action

Moreover, even if the bare assertion of the Office Action is correct, which Applicant does not admit, such assertion does not anticipate the claims of instant Group I and thus does not destroy unity of invention as between Groups I and IV. The claims of Group I are directed to a process for generating a combinatorial set of molecules of core structure M by:

- (a) preparing a plurality of immobilized molecules of core structure M, wherein said molecules contain a plurality of reactive moieties, each reactive moiety being blocked by a blocking group, wherein at least three of the blocking groups are independently removable under at least three different conditions, and
- (b) removing certain blocking groups and derivatizing the resulting reactive moieties in a preprogrammed, regioselective manner, wherein each member of a combinatorial set is uniquely derivatized

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at at least one reactive moiety with a unique substituent, thereby generating a combinatorial set of molecules of core structure M.

It is respectfully submitted that the bare allegation of the Office Action does not anticipate this claim. Instant claim 1 requires use of three blocking groups that are independently removable under at least three different conditions in a preprogrammed, regioselective manner. Furthermore, instant claim 1 requires that each member of the combinatorial set produced by the claimed process be uniquely derivatized at at least one reactive moiety with a unique substituent. The bare allegation of the Office Action that "it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups" does not recite these limitations. Therefore, the bare allegation of the Office Action, if accepted as true, does not anticipate the claims of instant Group I, and also does not destroy the unity of invention as between Groups I and IV.

Applicant respectfully petitions for removal of the lack of unity objection as between Groups I and IV, and that these Groups be combined for examination in the instant application.

The finality of the Objection is premature

Furthermore, irrespective of whether the arguments presented in the Office Action are correct or not, the finality of the Objection is premature. The Office Action alleges for the first time that "it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups." Thus, the Office Action has provided a new basis for the allegation of lack of unity of invention while simultaneously making the Objection final. Applicant has not been provided an opportunity to respond to the new basis for the Objection. Therefore, it is respectfully submitted that the finality of the Objection is premature.

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Summary

Applicant petitions for removal of the lack of unity objection as between Groups I and IV. It is respectfully submitted that the Objection as between Groups I and IV is improper because the Groups are related as a product and a process specially adapted for preparation of the product. Such related Groups do not lack unity of invention within the meaning of PCT Rule 13.1.

Furthermore, the bare assertion of the Office Action does not anticipate the claims of instant Group I, and, therefore, does not destroy the unity of invention as between Groups I and IV. Also, the finality of the Objection is premature because Applicant has not had the opportunity to respond to the new basis for the Objection set forth in the Office Action.

REQUIREMENT FOR ELECTION OF SPECIES

Applicant respectfully requests removal of the Requirement for Election of Species. It is respectfully submitted that, as described in detail below, the species are so linked as to form a single general inventive concept within the meaning of PCT Rule 13.1 (see, MPEP 1893.03(d)). It is noted that nothing herein should be construed as an admission that the various species present in the instant claims are obvious variants of each other. Furthermore, it is respectfully submitted that the requirement for election of a single species is inconsistent with the subject matter of the instant claims.

Unity of Invention

This application is the U.S. national stage of International Patent Application No. PCT/US97/06509. Therefore, PCT regulations with respect to unity of invention are applicable herein (see, PCT Rule 13, 37 CFR §1.475, and MPEP 1893.03(d)). Unity of invention is based on the basic principle that an applicant has the right to include in a single application those inventions (e.g., species) which are so linked as to form a single general inventive concept (MPEP 1893.03(d)). Applicant respectfully submits that, given the subject matter of the instant claims, the building blocks (e.g., nucleosides), reactive

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groups, and protecting groups are so linked as to form a single general inventive concept. Therefore, a requirement to elect a single species in each of these elements is inappropriate.

The instant claims are directed to a combinatorial protecting group strategy for multifunctional molecules. In particular, the claims are directed to products and processes for oligonucleotide synthesis and for preparation of combinatorial libraries. Restriction of the claims to the single species required in the Office Action would negate a fundamental aspect of the subject matter of the instant claims (i.e., the combinatorial aspect).

Restriction of Monomers

The instant claims are directed to products and processes for preparation of the products, where the products are a combinatorial set of molecules of core structure M, or a composition comprising an oligomer. In particular, the claims are directed to (1) oligomers comprising not only of one moiety, but in the case of oligonucleotides, of at least all four of the natural building blocks, and (2) within the oligomer, using different protecting groups at different positions within the oligomer chain (even at the same type of building block).

As described in detail in the application, such products are useful as drugs. Modified oligonucleotides are used in an antisense/triplex DNA approach. Modifications are necessary to provide oligonucleotides of desired cell and nuclear transport properties, while retaining the desired activity. The instant processes provide such various products in a preprogrammed, specific manner requiring only one oligonucleotide synthesis run. In order to fully utilize the products and processes of the instant claims, use of various monomers is required.

Therefore, restriction of the claims to only a single building block, particularly where the products are oligonucleotides, (e.g., a single disclosed species from claim 10; a single disclosed species representing B or B^{R2A} or B^{R2B}; or a single disclosed species from claim 31) is not appropriate since these

building blocks are all part of a single general inventive concept. The claims are directed to compositions and combinatorial libraries containing oligonucleotides, and processes for preparation of same. If Applicant were required to elect a single disclosed nucleoside species as required, then the search, and any resulting allowed claims, would be limited to oligonucleotides containing only the single elected nucleoside (i.e., TTTTTTT..., GGGGGG..., AAAAAA..., CCCCCC..., etc.). Such a requirement is inconsistent with the subject matter of the instant claims, and violates Applicant's right to have all species that form a single general inventive concept included in a single application.

Restriction of Reactive Groups and Protecting Groups

Furthermore, the application is directed to a combinatorial protecting group strategy for multifunctional molecules. Restriction to a single reactive group or a single protecting group is inconsistent with the subject matter of the instant claims.

Restriction of the claims to only a single reactive group, e.g., a reactive group of claims 11 or 24, is not appropriate because the claims are directed to products and processes that have different protecting groups at different positions (i.e., on different reactive groups) within the product. To restrict the reactive groups to a single reactive group would negate a fundamental aspect of the instant claims. The different reactive groups are part of the single general inventive concept of the instant claims.

Restriction of the claims to only a single protecting group, e.g., a single R^{4A} or R^{4B} group; or a single R^{2A} or R^{2B} group; or a single group for R^3 ; is also not appropriate because the claims are directed to different protecting groups at different positions within the product. To restrict the reactive groups to a single reactive group would negate a fundamental aspect of the instant claims. The different protecting groups are part of the single general inventive concept of the instant claims.

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Therefore, requiring election of a single disclosed reactive group or protecting group is inconsistent with the subject matter of the instant claims. Moreover, such requirement violates Applicant's right to have all species that form a single general inventive concept included in a single application (see, MPEP 1893.03(d)).

Summary

For the reasons given above, Applicant respectfully requests removal of the lack of unity objection as between Groups I and IV. Furthermore, Applicant respectfully requests removal of the lack of unity objection as relating to the requirement for election of a single species.

* * *

Respectfully submitted,
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